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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/445,576	07/17/2000	HANS CHRISTIAN THOGERSEN	THOGERSEN=1	1127

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EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 12/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/445,576	Thorgersen et al
Examiner	**Art Unit**
Karen Canella	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 19, 22, 23, and 68-134* is/are pending in the application.

4a) Of the above, claim(s) *92, 93, 95-97, 100, 101, 104, and 105* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 19, 22, 23, 68-91, 94, 98, 99, 102, 103, and 106-134* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Response to Amendment

1. Claim 24 has been canceled. Claims 106-134 have been added. Claims 1, 19, 22, 23 and 68-134 are pending. Claims 92, 93, 95-97, 100, 101, 104 and 105, drawn to non-elected inventions, remain withdrawn from consideration. Claims 1, 19, 22, 23, 68-80, 81 82-91 94 and 98, 99, 102, 103 and 106-134 are under consideration. KAC 5/7/03

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

3. The objection under 35 U.S.C. 132 to the amendments filed March 1, 2002 and February 2, 2001 because they introduce new matter into the disclosure. Is withdrawn in light of applicants amendments.

4. The amendment filed December 2, 2002 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: Figure 2 has been amended to substitute "X" for "hy". The specification as filed defined "hy" as a hydophobic aliphatic amino acid residue. Substitution of "X" alters the scope of the consensus sequence defined comprising "hy" as originally filed..

Applicant is required to cancel the new matter in the reply to this Office Action.

5. Claims 80 and 82 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 80 recites "a repeated heptad having the formula a-b-c-d-e-f-g". It is unclear if this represents a single amino acid sequence, or a collection of amino acid sequences. If applicant intends to claim a collection of amino acid sequences, it is unclear what constitutes an a residue, a b residue a c residue, etc. For purpose of examination, the formula a-b-c-d-e-f-g will be interpreted as a single amino acid sequence and as a collection of amino acid sequences.

The term "substantially" in claim 82 is a relative term which renders the claim indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. .

6. Claims 80 and 81 are objected to as not complying with 1.821(d) of the Sequence Rules and Regulations. For the reasons set forth above, the heptad of a-b-c-d-e-f-g represents an amino acid sequence that is encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, said amino acid sequence is not labeled with a sequence identifier as required. Appropriate correction is required.

7. The rejection of claims 1, 19, 68-77, 83, 86, 88, 90 and 98 under 35 U.S.C. 102(b) as being anticipated by Thogersen et al (WO 94/18227, reference AA of the IDS filed April 23, 2001) as evidenced by Kastrup et al (Acta Cryst, January 1997, Vol. D53, pp. 108-111, reference AX of the IDS filed April 23, 2001) and as evidenced by the abstract of Nielsen et al (FEBS Lett 1997, vol. 412, pp. 388-396, reference BC of the IDS filed April 23, 2001) is withdrawn in light of applicants arguments.

8. The rejection of claims 22, 23, 68-77, 82-90, 94, 98, 99, 102 and 103 under 35 U.S.C. 103(a) as being unpatentable over Thogersen et al (WO 94/18227, reference AA of the IDS filed April 23, 2001), Kastrup et al (Acta Cryst, January 1997, Vol. D53, pp. 108-111, reference AX of the IDS filed April 23, 2001), in view of Hoppe et al (WO 95/31540, reference AB of the IDS filed April 23, 2001) is withdrawn in l;ight of applicants arguments.

9. The rejection of claims 22, 23, 68-77, 82-91, 94, 102 and 103 under 35 U.S.C. 103(a) as being unpatentable over Thogersen et al (WO 94/18227, reference AA of the IDS filed April 23, 2001), and Kastrup et al (Acta Cryst, January 1997, Vol. D53, pp. 108-111, reference AX of the IDS filed April 23, 2001), and the abstract of Nielsen et al (FEBS Lett 1997, vol. 412, pp. 388-396, reference BC of the IDS filed April 23, 2001) in view of Hoppe et al (WO 95/31540, reference AB of the IDS filed April 23, 2001) as applied to claims 22, 23, 68-77, 82-90, 94, 102

and 103 above, and further in view of Baker et al (US 5,627,073) is withdrawn in light of applicants arguments.

10. Claims 1, 19, 22, 23, are rejected under 35 U.S.C. 102(b) as being anticipated by Hoppe et al (WO 95/31540, cited in a previous Office action).

Claim 1 is drawn to a monomer peptide construct comprising at least one tetranectin trimerizing structural element (TTSE), which is linked to a heterologous moiety, said TTSE capable of forming a stable triple alpha helical coiled-coil complex with two other TTSE. Claim 1 (and page 7, lines 6-17 of the instant specification) further excludes fusion proteins taught in the prior art, said fusion proteins made to facilitate expression and/or purification of said monomer peptide construct. The specification defines the tetranectin trimerizing structural element on page 14, lines 1-10 as a portion of the polypeptide molecule of the tetranectin family which is responsible for trimerization between monomers of the tetranectin polypeptide . The term is also intended to embrace variants of a TTSE of a naturally occurring tetranectin family member, variants which have been modified in the amino acid sequence without adverse affecting to any substantial degree , the trimerization properties relative to those of the native tetranectin monomer. . The specification define a tetranectin family member on page 17, lines 5-7 as a polypeptide which shares the consensus sequence shown in figure 2 or a sequences which are homologous at the sequence level with this consensus sequence. The specification states preferred embodiemsnts of homologus sequences that are 68%, 75% or at least 92% identical to

the consensus sequence. It is noted that these are preferred embodiments and do not constitute limits on the scope of a homologous sequence. Dependent claim 19 is drawn to an oligomer comprising at least two monomer peptide constructs according to claim 1. The specification defines oligomer on page 19, lines 6-10, as being a non-covalent complex of two or more monomer peptide constructs.

Claim 19 is drawn to a trimeric polypeptide complex comprising three monomer peptides wherein each of said monomer polypeptides comprises a TTSE, said TTSE being a polypeptide having at least 68% sequence identity with the consensus sequence shown in Figure 2, and at least one of said monomer polypeptides is covalently linked to a heterologous moiety.

Claim 22 is drawn to the trimeric polypeptide complex of claim 68, wherein the at least one heterologous moiety is positioned N-terminally to the TTSE and the at least one heterologous moiety is positioned C-terminally to the TTSE are on the same monomer polypeptide. Claim 23 is drawn to the trimeric polypeptide complex of claim 68, wherein the at least one heterologous moiety is positioned N-terminally to the TTSE and the at least one heterologous moiety is positioned C-terminally to the TTSE are on the separate monomer polypeptides.

Hoppe et al disclose a collectin neck region polypeptide or a variant or derivative thereof or a sequence of amino acids having an amino acid pattern or hydrophobicity profile which is the same as or similar to that of the collectin neck region and able to form a timer (page 3, lines 12-16). Hoppe et al disclose heterologous moieties positioned at the N or C terminus of collectin (page 6, lines 15-18 and page 12, lines 4-13). Because of the definition in the specification which

encompasses proteins having homologous sequences to the disclosed neck region of human tetranectin, the disclosure of collectin is encompassed by claims drawn to tetranectin trimerizing element.

11. Claims 1, 19, 22, 23, 68-91, 94, 98, 99, 102, 103, 106-134 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoppe et al (WO 95/31540) in view of Thogersen et al (WO 94/18227, reference AA of the IDS filed April 23, 2001) as evidenced by Kastrup et al (Acta Cryst, January 1997, Vol. D53, pp. 108-111, reference AX of the IDS filed April 23, 2001) and as evidenced by the abstract of Nielsen et al (FEBS Lett 1997, vol. 412, pp. 388-396, reference BC of the IDS filed April 23, 2001).

Hoppe et al teach collectin as a trimerizing molecule which can be fused to heterologous moieties on the N or C termini. Hoppe et al teach that this trimerized structure is stable at temperatures of 50 degrees C. Hoppe et al do not teach a tetranectin variant having a neck region that is at least 68% identical to the consensus sequence in figure 2.

Thogersen et al, as evidenced by Kastrup et al, teach that tetranectin forms trimers in solution and in the crystal state. Thogersen et al teach that the oligomerization of the tetranectin monomer is not interrupted by a heterologous moiety fused N-terminally to the tetranectin polypeptide. Kastrup et al teach that the structural feature of tetranectin responsible for trimerization is in the polypeptide encoded by exons 1 and 2 of the tetranectin gene (page 111, last sentence). Kastrup et al compares full length tetranectin with mannose binding protein which

also has trimerizing ability. Kastrup et al points out that the neck region of mannose binding protein has been shown to be responsible for stabilization of the conformation of the C-terminal part of the timer. Thus, one of skill in the art would conclude that the sequence of Thorgersen et al is a trimerizing structural element having 100% sequence identity to the consensus sequence in figure 2. Claim 1 specifically recites that the heterologous moiety is different from the fusion proteins as found in Thogersen et al.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to use the tetranectin neck region in place of the collectin neck region. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Kastrup et l on the trimerization, rather than tetramerization, afforded by the tetranectin neck region.

Conclusion

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella, Ph.D.

Patent Examiner, Group 1642

May 20, 2002